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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,190	10/31/2003	Barbara Grimpe	CWRU-P01-018	1183

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,190	GRIMPE ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-54* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-28, 29-34, and 36 drawn to methods of reducing GAG content in a glial scar and methods of promoting neuronal regeneration and methods of screening agents, classified in class 536, subclass 24.5 and class 514, subclass 44 and class 435, subclass 9.1.

If Group I is elected, a species election is required. It is necessary for the applicants' to elect one of the distinct species of Agent selected from the group consisting of:

Ia. Antisense oligonucleotides, as recited in claims 6, 9, 15, 20 and 32;

Ib. Ribozymes, as recited in claims 6, 9, 15, 20 and 32;

Ic. DNA enzymes, as recited in claims 6, 9, 15, 20 and 32;

Id. RNAi, as recited in claims 6, 9, 15, 20 and 32;

Ie. Small molecules, as recited in claims 6, 9, 15, 20 and 32;

If. Antagonists, as recited in claims 9, 15, 20 and 32;

Ig. Antibodies, as recited in claims 9, 15, 20 and 32;

Claims 1-5, 7-8, 10-14, 16-19, 21-31, 33-34, and 36 link(s) species of Agents. The restriction requirement among the linked claims is subject to the nonallowance of the linking claims 1-5, 7-8, 10-14, 16-19, 21-31, 33-34, and 36. Upon the indication of

allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct because each of the molecules recited in Group I are classified as structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleic acid and amino acid sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

There is a burdensome search associated with the member of this species grouping. For example, the search for Antibodies would not discover Ribozymes. Further example, searching antisense oligonucleotides would not reveal small molecules. Many of these classes of molecules are so different from each other, that only a lengthy search of many unrelated databases could disclose all members included in the categories asserted by the inventors' application.

After an Agent type has been elected, another species election is necessary. For *each of the three categories* listed below, the applicant must elect one SEQ ID NO from those listed in generic claims 7, 10, 11, 13, 16, 21, 22, and 24 and designate which SEQ ID NO corresponds to molecules that are capable of:

--inhibiting the expression of primary proteoglycans,

--inhibiting the expression and/or activity of a chain initiation enzyme,

--inhibiting the expression and/or activity of a chain elongation enzyme,

Claims of Invention I are written such that embodiments may include one or more of the inhibitors of expression. This election of three different types (inhibitors of proteoglycans, chain initiators, and chain elongators) of SEQ ID NOs will allow complete examination of the full scope of the claimed Invention I.

The species are independent or distinct because each of these nucleic acids has a unique structure that is distinct from all of the others. Since each nucleic acid sequence has a unique structure, they are considered distinct chemical compounds and

are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleic acid presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

There is a burdensome search for the examiner associated with searching members of this species grouping. The numerous sequences claimed in this application are so different from each other, that only a lengthy search of many databases could disclose all members included in the inventors' application.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for each of the three categories of inhibitor, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claims (7, 10, 11, 13, 16, 21, 22, and 24), applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

In addition, to the species elections above, in order to examine the neuroregenerative aspect of Invention I, an additional species election is necessary. Claims 17 and 25 are generic to a plurality of disclosed patentably distinct species of growth factors or neurotropic factors selected from the group consisting of:

I-1. nerve growth factor, as recited in claim 26;

I-2. brain-derived growth factor, as recited in claim 26;

I-3. neurotrophin 3, as recited in claims claim 26;

I-4. neurotrophin 4, as recited in claims claim 26;

I-5. neurotrophin 5, as recited in claims claim 26;

I-6. glial derived neurotropic factor, as recited in claims claim 26;

I-7. ciliary neurotrophic factor, as recited in claim 26;

I-8. fibroblast growth factor, as recited in claim 27.

The inventions are distinct each from the other because different proteins having different amino acid sequences are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such amino acid sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

Because these inventions are structurally distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject

matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated.

There is a burdensome search for the examiner associated with these species. Many of these molecules are sufficiently different from each other, that an extensive search of databases be required to disclose all members included in the species group.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

II. Claim 38, drawn to methods of manufacture of a medicament using a DNA enzyme agent, classified in class 536, subclass 23.1.

III. Claim 39, drawn to methods of manufacture of a medicament using an antisense oligonucleotide agent, classified in class 536, subclass 23.1

IV. Claims 35, 37, 40, 42-45, 46, 48-53 drawn to a composition comprising a DNA enzyme agent or RNAi agent, pharmaceutical preparation thereof, and kit comprising said preparation, classified in class 536, subclass 23.1, class 536, subclass 24.5, class 514, subclass 44 and class 206, subclass 223

V. Claims 35, 37, 41, 43-35, 47, drawn to a composition comprising an antisense oligonucleotide agent, pharmaceutical preparation thereof, and kit comprising said preparation, classified in class 536, subclass 24.5, class 514, subclass 44 and class 206, subclass 223

Invention Distinctions

2. The inventions are independent or distinct, each from the other because:

The Product Inventions (IV and V) to related the Process Inventions (I-III). The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, Inventions IV-V are nucleic acid molecules that are used in or by

Inventions I-III. The method Invention I, reducing GAG content in glial scars and promoting neural regeneration and methods of screening, could be accomplished with molecules other than Inventions IV-V, such as with nerve growth factors. Methods of manufacturing a medicament to inhibit expression or activity of xylotransferase (Inventions II-III) can be accomplished without using Inventions IV-V, such as using small molecules, peptides and hormones. For the reasons given above, Inventions IV-V are distinct from Inventions I-III and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Inventions IV-V are related but distinct products. Each of these inventions are nucleic acids, but they have different design, mode of operation, function or effect. DNA enzymes (Invention IV) recognize a target nucleic acid and cleave the target nucleic acid, and RNAi is double stranded RNA that encourages mRNA degradation through a less than fully characterized mechanism that does not involve binding to the mRNA. . Antisense nucleic acids (Invention V) bind to mRNAs with complementary sequences and consequently, triggers degradation of a particular message. Because of the reasons given above, and the search burden inherent in the searches of different classes of molecules, restriction is required.

Inventions I-III are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive;

the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). Groups I-III are different methods. Methods of (1) reducing GAG content in a glial scar and promoting neuronal regeneration, (2) screening to identify or characterize an agent, (3) manufacturing medicaments (Inventions II & III) differ with respect to reagents, method steps, and endpoints. Each of the methods contains differences from the other that make them distinct and non-overlapping, (1) unique reagents, including specific SEQ ID NOs and the use of neurotropic factors, (2) screening libraries of compounds, (3) the manufacturing steps are not treated in depth in the specification, but it is assumed that the process for manufacturing would include many common in the various arts, such as fermentation of bacteria containing plasmids, which are different steps from Inventions I. The searches of these methods require distinct queries and would not overlap. Therefore the examiner would experience undue burden and restriction is required.

Inventions II and III include claims (38-39) that are difficult for the examiner to understand. The "use of an agent" is non-statutory invention class. The examiner is interpreting Claims 38-39 to be method claims. If this was the intent of the applicant, it is recommended that the language of these claims be amended.

Inventions II and III Inventions are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the

inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the DNA enzymes have a catalytic activity that is not present in the antisense oligonucleotides. For this reason these molecules are considered to have different modes of operation and require restriction. The search for these different classes of molecules is burdensome.

Because these inventions are independent or distinct for the reasons given above and have acquired a separate status in the art in view of their different classification, or divergent subject matter, or the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Notice of Possible Rejoinder

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Response Requirement

4. Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Multiple Inventors

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Examiner Contact Information

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave Nguyen** can be reached on **571-272-0731**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER

Scott Long
Art Unit 1633